

REMARKS

Favorable consideration and allowance are respectfully requested for claims 1-5 in view of the following remarks and the Declaration of Dr. Heinz Rupp, enclosed herewith.

As he explains in his Declaration, Dr. Rupp is a highly qualified expert in the field of cardiology and cardiac function. Dr. Rupp is an author or co-author on over 130 scientific publications the majority of which are directly related to cardiology and cardiac function. Further Dr. Rupp has been engaged in the field of cardiovascular sciences since 1979 and is a Professor of Physiology in the Department of Internal Medicine and Cardiology at the Phillipps University of Marburg in Marburg, Germany. Given Dr. Rupp's experience and education he is certain one skilled in the art.

Rejection Under 35 U.S.C. §§ 102(b) and 103(a) over WO 97-46241

Claims 1-5 were rejected under 35 U.S.C. § 102(b) as being anticipated by WO 97-46241 (the '241 application). Claims 1-5 were also rejected under 35 U.S.C. § 103(a) over the '241 application. These rejections are respectively traversed.

The present claims are directed to a method of treating postmyocardial infarction through administration of moxonidine or a physiologically compatible salt thereof.

The '241 application relates to the hemodynamic parameters associated with congestive heart failure. As explained in the enclosed Declaration of Dr. Heinz Rupp, "[t]here is no information provided in the '241 application regarding the treatment or inhibition of myocardial damage secondary to myocardial infarction." See Paragraph 13 of the Declaration. The Office Action indicates that the '241 application "does not exclusively state postmyocardial infarction or recovery of myocardial status, as claimed." (See Page 3 of the Office Action). In

fact, the '241 application makes no reference to treatments for postmyocardial infarction or recovery of myocardial status, and relates only to treatment of congestive heart failure. The lack of such a reference in the '241 application is significant, because of the difference in the goals of treating congestive heart failure when compared with inhibiting damage after myocardial infarction, and because of the wide variety of causes of congestive heart failure.

In his Declaration, Dr. Rupp explains the differences in the treatment goals for addressing congestive heart failure and for inhibiting damage after myocardial infarction. In Paragraph 14 of the Declaration, Dr. Rupp explains that treatments for congestive heart failure are targeted at improving the function of the heart. Congestive heart failure may be defined as the inability of the heart to supply the bodily demands for sufficient blood. See Paragraph 14. Avoiding further myocardial damage following myocardial infarction is not related to improving cardiac function, rather it relates to preserving primary ischemic myocardium and inhibiting necrosis. See the first paragraph on page 3 of the Specification. Because of this difference, one skilled in the art would not be motivated to modify treatments for congestive heart failure when trying to arrive at suitable treatments for postmyocardial infarction. There is no suggestion anywhere in the '241 application that would lead one skilled in the art to expect that administration of moxonidine following myocardial infarction would inhibit further myocardial damage.

The Declaration of Dr. Rupp also explains that congestive heart failure may be caused by a wide variety of mechanisms or conditions. Acute myocardial infarction is only one of these causal mechanisms or conditions. Dr. Rupp explains that just as it is improper to assume "that a treatment for congestive heart failure is suitable for treating all of the . . . mechanisms or conditions which may precede congestive heart failure, it is similarly improper to assume that the method of treating congestive heart failure taught in the '241

application would be proper or even beneficial in treating a postmyocardial infarction patient." See Paragraph 13 of the Declaration.

After careful review of the '241 application, Dr. Rupp determined that the '241 application provides no teaching or suggestion to administer moxonidine to inhibit damage secondary to myocardial infarction. See Paragraphs 13 and 15 of the Declaration. Because the '241 application is limited to treatments of congestive heart failure (see Paragraphs 13 and 15 of the Declaration) and because treatments for congestive heart failure are targeted at improving heart function, and cannot be assumed to be beneficial or even suitable to inhibit damage secondary to myocardial infarction (see Paragraphs 13, 14 and 15 of the Declaration), and because there are a wide variety of causal factors that lead to congestive heart failure (as Dr. Rupp notes in Paragraph 13) which are not known to lead to postmyocardial infarction damage, Dr. Rupp determined that the '241 application does not provide a person skilled in the art any motivation to try to inhibit myocardial damage by administering moxonidine following myocardial infarction. See Paragraph 15 of the Declaration. This clearly demonstrates that the '241 application does not teach or suggest or provide any motivation to administer moxonidine to inhibit myocardial damage secondary to myocardial infarction.

As explained in the Manual of Patent Examining Procedure (MPEP), in order to anticipate a claim under 35 U.S.C. 102(b), a reference must teach every element of the claim. See the MPEP § 2131. Patent and Trademark Office, U.S. Department of Commerce, *Manual of Patent Examining Procedures* (8<sup>th</sup> Edition, August, 2001). In order to establish a *prima facia* case of obviousness, a rejection under 35 U.S.C. § 103 requires that there be some motivation or suggestion to one skilled in the art to modify the reference and that the cited prior art teach or suggest all of the application's claim limitations. See the MPEP at § 706.03(j).

The '241 application does not teach a method of treating a patient who has suffered a myocardial infarction to inhibit myocardial damage secondary to myocardial infarction as is required in claim 1. Similarly, the '241 application does not teach treating myocardial damage secondary to myocardial infarction in acute myocardial infarction as is required in claim 2. The '241 application does not teach postmyocardial infarction management or the management of chronic postmyocardial infarction patients, as is set forth in claims 3 and 4. The '241 application also provides no teaching or motivation to treat myocardial damage secondary to myocardial infarction with an amount of the compound of Formula I or physiologically compatible salt thereof that is effective in promoting recovery or rehabilitation of myocardial status as is described in claim 5.

Thus, pending claims 1-5 include elements which are not disclosed and are not suggested by the '241 application. Further the '241 application provides no motivation or suggestion for a person skilled in the art to try to modify the methods taught in the '241 application as would be necessary to arrive at the presently claimed invention.

As a result of this failure to teach or suggest or provide motivation to arrive at all of the elements of the presently pending claims, the rejections of claims 1-5 under 35 U.S.C. §§ 102(b) and 103(a) cannot be properly maintained.

It is respectfully requested that these rejections be withdrawn.

Rejections Under 35 U.S.C. §§ 102(b) and 103(a) in view of Lepran

Claims 1-5 were rejected under 35 U.S.C. § 102(b) and 103(a) over Lepran. et al. (J. Cardiovascular Pharmacology, 1994). As explained in the Declaration of Dr. Rupp, the Lepran article does not teach or suggest administering moxonidine to inhibit postmyocardial infarction damage or to recover myocardial status. The "damage" of the present claims is related to actual myocardial damage in a postmyocardial infarction patient. While the arrhythmias or ventricular fibrillation discussed in the Lepran article represent abnormal heart operation,

they do not necessarily indicate myocardial damage. Therefore, treatment to inhibit myocardial damage following myocardial infarction which will recover myocardial status is separate and distinct from treatment for arrhythmias or ventricular fibrillation.

As explained in the Declaration of Dr. Rupp, all the methods of the Lepran article rely on administration of moxonidine *before* coronary ligation leading to either myocardial infarction or myocardial ischemia. All the claims of the present application, however, are directed to treatment of a patient *after* a myocardial infarction. As indicated in the quotation from the Lepran article provided at the top of page 7 of Dr. Rupp's Declaration, the authors of the Lepran article understood their results to indicate that moxonidine may be useful if administered so that it is present **during** an acute myocardial infarction. Thus, the Lepran article teaches that the physiological presence of moxonidine during an evolving myocardial infarction may be beneficial. This is separate and distinct from inhibiting damage after a myocardial infarction. The Lepran article provides no suggestion or motivation to one skilled in the art that moxonidine administration *after* myocardial infarction might be beneficial in inhibiting damage as is presently claimed. As a result, Dr. Rupp correctly concludes that "the subject matter of the claims of the present application is not described by the Lepran article." See Paragraph 17 of the Declaration.

The Lepran article does not teach a method of treating a patient who has suffered a myocardial infarction to inhibit myocardial damage secondary to myocardial infarction as is required in claim 1. Similarly, the Lepran article does not teach treating myocardial damage secondary to myocardial infarction in acute myocardial infarction as is required in claim 2. The Lepran article does not teach postmyocardial infarction management or the management of chronic postmyocardial infarction patients, as is set forth in claims 3 and 4. The Lepran article also provides no teaching or motivation to treat myocardial damage secondary to myocardial infarction with an amount of the compound of Formula I

or physiologically compatible salt thereof that is effective in promoting recovery or rehabilitation of myocardial status as is described in claim 5.

The Lepran article provides no suggest or motivation to modify the method of administering of moxonidine *before* coronary ligation leading to either myocardial infarction or myocardial ischemia so as to arrive at the claimed method of administering moxonidine *after* myocardial infarction. Even further, the Lepran article certainly does not provide any suggestion or motivation to try to inhibit postmyocardial damage through administration of moxonidine after myocardial infarction.

In order to anticipate a claim under 35 U.S.C. § 102(b), a reference must teach every element of the claim. See the MPEP § 2131. Patent and Trademark Office, U.S. Department of Commerce, *Manual of Patent Examining Procedures* (8<sup>th</sup> Edition, August, 2001). In order to establish a *prima facia* case of obviousness, a rejection under 35 U.S.C. § 103 requires that there be some motivation or suggestion to one skilled in the art to modify the reference and that the cited prior art teach or suggest all of the application's claim limitations. See the MPEP at § 706.03(j).

As explained above, the Lepran article fails to teach all of the elements of the presently claimed methods, and provides no suggestion or motivation to one skilled in the art to modify the methods to arrive at the presently claimed invention. Therefore, the rejections under 102(b) and 103(a) cannot be properly maintained.

Withdrawal of these rejections is respectfully requested.

Dr. Rupp concludes that "no currently available therapy for postmyocardial infarction patients provides any suggestion or motivation to administer moxonidine to inhibit damage secondary to myocardial infarction or to provide myocardial recovery following myocardial infarction." As a result, the

claims of the present application describe what are clearly novel and nonobvious methods. For at least the foregoing reasons, these claims are allowable.

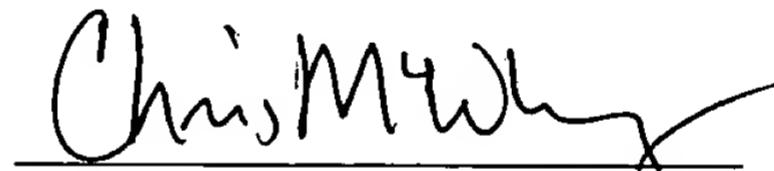
### CONCLUSION

In view of the foregoing, the application is respectfully submitted to be in condition for allowance, and prompt favorable action thereon is earnestly solicited.

If there are any questions regarding this amendment or the application in general, a telephone call to the undersigned would be appreciated since this should expedite the prosecution of the application for all concerned.

Although a petition for an Extension of time is submitted herewith, if necessary to effect a timely response, this paper should be considered as a petition for an Extension of Time sufficient to effect a timely response, and please charge any deficiency in fees or credit any overpayments to Deposit Account No. 05-1323 (Docket No. 147/50194).

Respectfully submitted,



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